REMARKS

Claims 50, 52-56, 58, 59, and 61 are pending in this application.

Claims 50, 55, and 58 are amended to further define the present invention.

Claims 1-49, 51, 57, 60 and 62-65 have been cancelled without prejudice in previous amendments.

Claims 50, 55, and 58 are amended to specify that not more than about 1 percent of the cells of the stem cell population express Tie-2. Support for this amendment can be found in the specification on page 8, lines 8-9; page 12, lines 9-10; and page 19, lines 15-18. No new matter is added by this amendment.

Claim 55 is amended further to specify that the stem cell population is a lineage negative hematopoietic stem cell population. Support for this amendment can be found in the specification on page 3, lines 9-13, page 10, lines 23-28. No new matter is added by this amendment.

Rejections Under 35 U.S.C. §112, Second Paragraph.

Claim 56 was rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for reciting "transfected lineage negative hematopoietic stem cell population of claim 55" without direct antecedent basis in claim 55 for this phrase. In response, claim 55 is amended to specify that the stem cell population is a lineage negative hematopoietic stem cell population. In view of the amendment to claim 55, Applicants request that the rejection of claim 56 for indefiniteness be withdrawn.

Rejections Under 35 U.S.C. §112, First Paragraph.

Method claims 55, 56, 58, 59, and 61 stand rejected under the first paragraph of 35 U.S.C. §112 as allegedly failing to comply with the enablement requirement, essentially for the same reasons stated in the Office Action dated March 16, 2005. As noted in Applicants response dated September 15, 2005, this rejection is in error and should be withdrawn. The gist of the rejection appears to be that the specification does not provide enough data to apprise one of ordinary skill in the art how to *make and use* the invention, with particular emphasis on *how to use*. The Office Action clearly applies the wrong standard for the how-to-use prong of enablement with respect to the present method claims. The how-to-use prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. §101

that the specification disclose as a matter of fact a practical utility for the invention. *In re Kirk*, 376 F.2d 936, 942, 153 U.S.P.Q. 48, 53 (CCPA 1967). The threshold of utility is not high. An invention is "useful" under §101 if it is capable of providing *some* benefit. *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 51 USPQ2d 1700 (Fed. Cir. 1999), emphasis added. Accordingly, all that is required for the how-to-use prong of enablement is that there be a teaching of "some benefit" for the claimed invention.

The present Office Action alleges that the "sole intended purpose for the methods as claimed is to attain therapeutic effects for ocular treatments". Such a characterization is unfair and unwarranted. The working examples in the present application clearly demonstrate a purpose for the present methods beyond attaining ocular therapeutic effects. One purpose for the present methods, clearly demonstrated to one of ordinary skill in the art by the present specification, is targeted delivery of operable genes to a specific tissue (e.g., the retina). As pointed out before, inhibition of angiogenesis is also a tool that can be used for research purposes (see, e.g., page 27, lines 19-25 of the specification). One of ordinary skill in the biotechnological art would immediately recognize such a utility, beyond therapeutic treatments, given the admittedly high level of skill in the art. A patent need not teach, and preferably omits, what is well known in the art. *Hybritech Inc. v. Monoclonal Antibodies, Inc.* 802 F.2d 1367, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986).

As noted above, the present claims are directed to methods of inhibiting angiogenesis in the eye of a mammal and to methods of delivering a gene encoding an antiangiogenic peptide to the eye. Both of these effects are clearly demonstrated, in animal models, by the working examples and data presented in the application. In addition, the specification clearly teaches how to isolate the stem cells, how to transfect them, and how to administer them to the eye. The application itself does demonstrate a "therapeutic effect" in the rd/rd mouse model, i.e., in delaying the onset of ocular degeneration to which these mice are genetically prone. That alone is enough to meet the threshold level of utility incorporated into the how-to-use prong of the enablement requirement (i.e., "some benefit"). Accordingly, the application does indeed teach one of ordinary skill in the art how to make and use the invention.

Furthermore, even if, *arguendo*, the claims are characterized as therapeutic

methods for treating an ocular disease, such treatment can be useful despite some potential adverse side affects in some subjects. An ocular treatment may be useful for some subjects even where only partial improvement in visual sensation is restored or where further degradation in vision is only slowed. There is no requirement in the law or in medicine that a treatment must be without some risk. Even great risk may be acceptable in some situations (e.g., where a subject is suffering from a terminal illness). The utility requirement also does not impose a requirement of commercial marketability. See *Studiengesellschaft Kohle v. Eastman Kodak Co.* 616 F.2d 1315, 1339, 206 U.S.P.Q. 577, 598 (5th Cir. 1980).

For the foregoing reasons, the rejection of claim 55, 56, 58, 59, and 61 for lack of enablement should be withdrawn.

Rejections Under 35 U.S.C. §103 (a).

Claims 50 and 52-54 stand rejected as being obvious over Wilson *et al.* in view of Schimmel *et al.* This rejection is unwarranted, as well. As recognized by the Examiner, Wilson *et al.* do not teach that the described stem cell population is transfected with a gene that encodes a therapeutically useful peptide.

The primary basis for this rejection is that Wilson *et al.* allegedly disclose the same stem cell population as the present application. That premise is incorrect. The stem cell population of Wilson *et al.* is different. The Wilson *et al.* cell population is highly expressive for the Tie-2 (also known as the TEK) cell marker, whereas the presently claimed cell population is not. According to Wilson *et al.*, 47% of the cells of the stem cell population express TEK (see col. 6, lines 45-67, particularly lines 54-55). In contrast, the stem cell population of the present invention is substantially Tie-2 negative. Less than about 1% of the cells express the Tie-2 cell marker (see page 12, lines 9-10and fig. 1, panel C). Claim 50 is amended to specify that not more than about 1% of the cells express Tie-2. Wilson *et al.* teach a different stem cell population than the present application. Accordingly, even if Wilson *et al.* and Schimmel *et al.* were combinable, the combined references do not teach or suggest all of the limitations of the present claims.

Furthermore, Schimmel *et al.* disclose that the T2 fragment of TrpRS is a potent antiangiogenic peptide. Schimmel *et al.* also disclose transfecting a cell line *for purposes of propagating therapeutic viral vectors.* Schimmel *et al.* do not teach or suggest

transfecting stem cells with a gene encoding T2-TrpRS. The only therapeutic vectors discussed by Schimmel *et al.* are viral vectors.

One of ordinary skill in the art would not have had a reasonable expectation of success in combining the teachings of Wilson *et al.* and Schimmel *et al.* to arrive at the presently claimed stem cell lines, since Wilson *et al.* teaches a different stem cell line, and Schimmel *et al.* deal only with viral vectors, not stem cells. Accordingly, Applicants request that this rejection be withdrawn.

Conclusion.

All of the present claims are supported by an enabling disclosure and are patentable over the applied art. Reconsideration of the finality of the rejection, early allowance of all pending claims, and passage of the application to issue is solicited. In the event the foregoing is deemed to be unpersuasive, Applicants request entry of the present amendment to place the claims in better form for appeal.

Respectfully submitted,

Dated: 20 April 2006

By /Talivaldis Cepuritis/
Talivaldis Cepuritis (Reg. No. 20,818)

OLSON & HIERL, LTD.
20 North Wacker Drive
36th Floor
Chicago, Illinois 60606
(312) 580-1180

CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this AMENDMENT AND RESPONSE UNDER RULE 116 is being transmitted by facsimile transmission to Fax No. 571-273-8300 on 20 April, 2006.

/Talivaldis Cepuritis/
Talivaldis Cepuritis (Reg. No. 20,818)